AMENDMENTS TO THE CLAIMS

Applicant submits below a complete listing of the current claims, including marked-up claims with insertions indicated by underlining and deletions indicated by strikethroughs and/or double bracketing. This listing of claims replaces all prior versions, and listings, of claims in the application:

Listing of the Claims

1. (Currently amended) A method for treating irritable bowel syndrome comprising administering to a patient in need of such treatment an amount of a pharmaceutical preparation comprising ~~a peripheral opioid antagonist~~ methylnaltrexone effective to ameliorate at least one symptom of the irritable bowel syndrome~~, wherein the pharmaceutical preparation is free of bioavailable calcium or salts thereof~~.

2. (Withdrawn) The method of claim 1 wherein the pharmaceutical preparation is administered parenterally.

3. (Canceled)

4. (Withdrawn - currently amended) The method of claim 1 [[~~3~~]] wherein the pharmaceutical preparation is administered intravenously.

5. (Withdrawn - currently amended) The method of claim 1 [[~~3~~]] wherein the pharmaceutical preparation is administered subcutaneously.

6. (Withdrawn - currently amended) The method of claim 1 [[3]] wherein the pharmaceutical preparation is administered via a needleless injection.

7. (Withdrawn - currently amended) The method of claim 1 [[3]] wherein the pharmaceutical preparation is administered via an infusion.

8. (Withdrawn) The method of claim 1 wherein the pharmaceutical preparation is administered intrarectally.

9. (Withdrawn) The method of claim 1 wherein the pharmaceutical preparation is administered transdermally.

10. (Withdrawn) The method of claim 1 wherein the pharmaceutical preparation is administered intranasally.

11. (Original) The method of claim 1 wherein the pharmaceutical preparation is administered as a solution.

12. (Withdrawn) The method of claim 1 wherein the pharmaceutical preparation is administered as a suppository.

13. (Withdrawn) The method of claim 1 wherein the pharmaceutical preparation is administered as an enema.

14. (Original) The method of claim 1 wherein the pharmaceutical preparation is administered as a tablet or capsule.

15. (Original) The method of claim 1 wherein the patient is not undergoing exogenous opioid treatment.

16. (Original) The method of claim 1 wherein the patient is female.

17. (Original) The method of claim 1 wherein the patient is male.

18. (Original) The method of claim 1 wherein the patient is a child.

19. (Original) The method of claim 1 wherein the symptom is diarrhea.

20. (Original) The method of claim 1 wherein the symptom is alternating constipation and diarrhea.

21. (Original) The method of claim 1 wherein the symptom is constipation.

22. (Original) The method of claim 1 wherein the symptom is constipation and abdominal pain.

23. (Original) The method of claim 1 wherein the symptom is abdominal bloating.

24. (Original) The method of claim 1 wherein the symptom is abdominal distension.

25. (Original) The method of claim 1 wherein the symptom is abnormal stool frequency.

26. (Original) The method of claim 1 wherein the symptom is abnormal stool consistency.

27. (Original) The method of claim 1 wherein the symptom is abdominal pain.

28. (Original) The method of claim 1 further comprising administering an antibiotic to the patient.

29. (Original) The method of claim 1 further comprising administering an opioid agonist to the patient.

30. (Original) The method of claim 1 further comprising administering at least one irritable bowel syndrome therapeutic agent to the patient.

31. (Original) The method of claim 30, further comprising administering an opioid agonist to the patient.

32. (Original) The method of claim 30, wherein the irritable bowel syndrome therapeutic agent is selected from the group consisting of antispasmodics, anti-muscarinics, antiinflammatory agents, pro-motility agents, $5HT_1$ agonists, $5HT_3$ antagonists, $5HT_4$ antagonists, $5HT_4$ agonists, bile salt sequestering agents, bulk-forming agents, alpha2-adrenergic agonists, mineral oils, antidepressants, herbal medicines, and combinations thereof.

33. (Withdrawn) The method of claim 30, wherein the irritable bowel syndrome agent is not a $5HT_3$ antagonist, a $5HT_4$ antagonist, or a $5HT_4$ agonist.

34. (Withdrawn) The method of claim 30 wherein the irritable bowel syndrome therapeutic agent is an antidiarrheal medication.

35. (Withdrawn) The method of claim 30 wherein the irritable bowel syndrome therapeutic agent is an antidepressant.

36. (Withdrawn) The method of claim 30 wherein the irritable bowel syndrome therapeutic agent is an herbal medicine.

37. (Withdrawn) The method of claim 30 wherein the irritable bowel syndrome therapeutic agent is an alpha$_2$-adrenergic agent.

38. (Original) The method of claim 30 wherein the agent is a $5HT_4$ agonist.

39. (Currently amended) The method of claim 38, wherein the $5HT_4$ agonist is 3-(5-methoxy-[[~~IM~~]]indole-3-yl-methylene)-N-pentylcarbazimidamide.

40. (Withdrawn) The method of claim 30 wherein the agent is polyethylene glycol 3350.

41. (Canceled)

42. (Canceled)

43. (Currently amended) The method of claim ~~41~~ 1 wherein the amount of ~~the quaternary derivative of noroxymorphone~~ methylnaltrexone ranges from 1.0 to 3.0 mg/kg.

44. (Canceled)

45. (Currently amended) The method of claim ~~41~~ 1 wherein the amount of ~~the peripheral opioid antagonist~~ methylnaltrexone ranges from 0.1 to 0.45 mg/kg.

46. (Canceled)

47. (Canceled)

48. (Withdrawn - currently amended) The method of claim ~~40~~ 1 wherein the amount of ~~peripheral opioid antagonist~~ methylnaltrexone is effective to achieve a mean peak plasma concentration of 1400 ng/ml or less.

49. (Withdrawn - currently amended) The method of claim 48 wherein the amount of methylnaltrexone is effective to achieve a mean peak plasma concentration ~~is~~ of 1200 ng/ml or less ~~of peripheral opioid antagonist~~.

50. (Withdrawn - currently amended) The method of claim ~~48~~ 49 wherein the amount of methylnaltrexone is effective to achieve a mean peak plasma concentration of 1000 ng/ml or less ~~of peripheral opioid antagonist~~.

51. (Currently amended) A method for treating irritable bowel syndrome comprising orally administering to a patient in need of such treatment an amount of a pharmaceutical preparation comprising ~~a peripheral opioid antagonist~~ methylnaltrexone effective to ameliorate at least one

symptom of the irritable bowel syndrome~~, wherein the pharmaceutical preparation is free of bioavailable calcium or salts thereof~~.

52. (Original) The method of any one of claim 51 wherein the pharmaceutical preparation is administered in an enteric coated formulation.

53. (Original) The method of any one of claim 51 wherein the pharmaceutical preparation is administered in a sustained release formulation.

54. (Original) The method of any one of claim 51 wherein the pharmaceutical preparation is administered in an enteric coated sustained release formulation.

55. (Original) The method of any of one claim 51 wherein the pharmaceutical preparation is administered in a colonic site-directed formulation.

56. (Original) The method of claim 51 wherein the patient is not undergoing exogenous opioid treatment.

57. (Original) The method of claim 51 wherein the patient is female.

58. (Original) The method of claim 51 wherein the patient is male.

59. (Original) The method of claim 51 wherein the patient is a child.

60. (Original) The method of claim 51 wherein the symptom is constipation.

61. (Original) The method of claim 51 wherein the symptom is constipation and abdominal pain.

62. (Original) The method of claim 51 wherein the symptom is diarrhea.

63. (Original) The method of claim 51 wherein the symptom is alternating constipation and diarrhea.

64. (Original) The method of claim 51 wherein the symptom is abdominal bloating.

65. (Original) The method of claim 51 wherein the symptom is abdominal distension.

66. (Original) The method of claim 51 wherein the symptom is abnormal stool frequency.

67. (Original) The method of claim 51 wherein the symptom is abnormal stool consistency.

68. (Original) The method of claim 51 wherein the symptom is abdominal pain.

69. (Original) The method of claim 51 further comprising administering an antibiotic to the patient.

70. (Original) The method of claim 51 further comprising administering at least one irritable bowel syndrome therapeutic agent.

71. (Withdrawn - currently amended) The method of claim ~~70~~ 115 wherein the irritable bowel syndrome therapeutic agent is an antidepressant.

72. (Withdrawn - currently amended) The method of claim ~~70~~ 115 wherein the irritable bowel syndrome therapeutic agent is an antidiarrheal medication.

73. (Withdrawn - currently amended) The method of claim ~~70~~ 115 wherein the irritable bowel syndrome therapeutic agent is a[[~~n~~]] herbal medicine.

74. (Withdrawn - currently amended) The method of claim ~~70~~ 51 wherein the pharmaceutical preparation further comprises ~~irritable bowel syndrome therapeutic agent is~~ an opioid agonist.

75. (Withdrawn - currently amended) The method of claim ~~70~~ 115 wherein the irritable bowel syndrome therapeutic agent is an alpha$_2$-adrenergic agonist~~agent~~.

76. (Currently amended) The method of claim ~~70~~ 115 wherein the irritable bowel syndrome therapeutic agent is a 5-HT$_4$ agonist.

77. (Currently amended) The method of claim ~~65~~ 76 wherein the 5-HT$_4$ agonist is 3-(5-methoxy-[[~~IM~~]]indole-3-yl-methylene)-N-pentylcarbazimidamide.

78. (Withdrawn - currently amended) The method of claim ~~70~~ 115 wherein the irritable bowel syndrome therapeutic agent is not a 5-HT$_3$ antagonist, a 5-HT$_4$ antagonist or a 5-HT$_4$ agonist.

79. (Withdrawn - currently amended) The method of claim ~~76~~ 115 wherein the irritable bowel syndrome therapeutic agent is a polyethylene glycol 3350.

80. (Canceled)

81. (Canceled)

82. (Currently amended) The method of claim ~~81~~ 51 wherein the amount of methylnaltrexone ranges from 50 to 750 mg/day.

83. (Currently amended) The method of claim ~~81~~ 82 wherein the amount of methylnaltrexone is 75 mg ~~of the quaternary derivative of noroxymorphone~~.

84. (Currently amended) The method of claim ~~81~~ 51 wherein the amount of methylnaltrexone is 225 mg ~~of the quaternary derivative of noroxymorphone~~.

85. (Currently amended) A pharmaceutical preparation comprising ~~a quaternary derivative of noroxymorphone and~~ methylnaltrexone, an irritable bowel syndrome therapeutic agent and a pharmaceutically acceptable carrier.

86. (Canceled)

87. (Canceled)

88. (Original) The pharmaceutical preparation of claim 85 wherein the irritable bowel syndrome therapeutic agent is selected from the group consisting of antispasmodics, anti-muscarinics, antiinflammatory agents, pro-motility agents, $5HT_1$ agonists, $5HT_3$ antagonists, $5HT_4$ antagonists, $5HT_4$ agonists, bile salt sequestering agents, bulk-forming agents, $alpha_2$-adrenergic agonists, mineral oils, antidepressants, herbal medicines and combinations thereof.

89. (Withdrawn - currently amended) The pharmaceutical preparation of claim ~~85~~ 88 wherein the irritable bowel syndrome therapeutic agent is an antispasmodic.

90. (Withdrawn - currently amended) The pharmaceutical preparation of claim ~~85~~ 88 wherein the irritable bowel syndrome therapeutic agent is an anti-muscarinic.

91. (Withdrawn - currently amended) The pharmaceutical preparation of claim ~~85~~ 88 wherein the irritable bowel syndrome therapeutic agent is an antiinflammatory agent.

92. (Withdrawn - currently amended) The pharmaceutical preparation of claim ~~85~~ 88 wherein the irritable bowel syndrome therapeutic agent is a pro-motility agent.

93. (Currently amended) The pharmaceutical preparation of claim ~~85~~ 88 wherein the irritable bowel syndrome therapeutic agent is a $5HT_1$ agonist, a $5HT_3$ antagonist or a $5HT_4$ agonist.

94. (Withdrawn - currently amended) The pharmaceutical preparation of claim ~~85~~ 88 wherein the irritable bowel syndrome therapeutic agent is not a $5HT_3$ antagonist, a $5HT_4$ antagonist or a $5HT_4$ agonist.

95. (Currently amended) The pharmaceutical preparation of claim ~~85~~ 88 wherein the irritable bowel syndrome therapeutic agent is a $5HT_4$ agonist.

96. (Currently amended) The pharmaceutical preparation of claim 95 wherein the irritable bowel syndrome therapeutic agent is 3-(5-methoxy-[[~~IM~~]]indole-3-yl-methylene)-N-pentylcarbazimidamide.

97. (Withdrawn - currently amended) The pharmaceutical preparation of claim ~~85~~ 88 wherein the irritable bowel syndrome therapeutic agent is a bile salt sequestering agent.

98. (Withdrawn - currently amended) The pharmaceutical preparation of claim ~~85~~ 88 wherein the irritable bowel syndrome therapeutic agent is a bulk-forming agent.

99. (Withdrawn - currently amended) The pharmaceutical preparation of claim ~~85~~ 88 wherein the irritable bowel syndrome therapeutic agent is an alpha2-adrenergic agonist.

100. (Withdrawn - currently amended) The pharmaceutical preparation of claim ~~85~~ 88 wherein the irritable bowel syndrome therapeutic agent is a mineral oil.

101. (Withdrawn - currently amended) The pharmaceutical preparation of claim ~~85~~ 88 wherein the irritable bowel syndrome therapeutic agent is an antidepressant.

102. (Withdrawn - currently amended) The pharmaceutical preparation of claim ~~85~~ 88 wherein the irritable bowel syndrome therapeutic agent is an herbal medicine.

103. (Previously presented) The pharmaceutical preparation of claim 85 wherein the pharmaceutical preparation is formulated for oral administration.

104. (Currently amended) The pharmaceutical preparation of claim ~~102~~ 103 wherein the formulation is selected from the group consisting of a capsule, a powder, a granule, a crystal, a tablet, a solution, an extract, a suspension, a soup, a syrup, an elixir, a tea, a liquid-filled capsule, an oil, a chewable tablet, a chewable piece, an enteric-coated tablet, a sustained release tablet or capsule, and an enteric-coated sustained release tablet.

105. (Withdrawn) The pharmaceutical preparation of claim 85 wherein the pharmaceutical preparation is formulated for rectal administration.

106. (Withdrawn) The pharmaceutical preparation of claim 105 wherein the formulation is selected from the group consisting of a suspension, a solution, a suppository, an oil, and an enema.

107. (Previously presented) The pharmaceutical preparation of claim 85 wherein the pharmaceutical preparation is formulated for a route of administration selected from the group consisting of sublingual, intranasal, transdermal, intradermal, intramuscular, subcutaneous, injectable, and infusion.

108. (Currently amended) A kit comprising:

a package containing ~~a peripheral opioid antagonist preparation~~ methylnaltrexone, ~~wherein the preparation is free of bioavailable calcium and salts thereof~~

an irritable bowel syndrome therapeutic agent; and

instructions for ~~using the preparation to treat~~ treating irritable bowel syndrome.

109. (Original) The kit of claim 108, further comprising an antibiotic.

110. (Currently amended) The kit of claim 108, further comprising an irritable bowel syndrome therapeutic agent.

111. (Previously presented) The kit of claim 108, wherein the preparation is a pharmaceutical preparation according to claim 85.

112. (Previously presented) The method of claim 38 wherein the $5HT_4$ agonist is tegaserod maleate.

113. (Previously presented) The method of claim 76 wherein the $5HT_4$ agonist is tegaserod maleate.

114. (Previously presented) The pharmaceutical preparation of claim 95 wherein the irritable bowel syndrome therapeutic agent is tegaserod maleate.

115. (New) The method of claim 70, wherein the irritable bowel syndrome therapeutic agent is selected from the group consisting of antispasmodics, antidiarrheal medications, anti-muscarinics, anti-inflammatory agents, pro-motility agents, $5HT_1$ agonists, $5HT_3$ antagonists, $5HT_4$ antagonists, $5HT_4$ agonists, bile salt sequestering agents, bulk-forming agents, alpha2-adrenergic agonists, mineral oils, polyethylene glycol 3350, antidepressants, herbal medicines, and combinations thereof.

116. (New) The pharmaceutical preparation of any of claims 1, 51, 85 or 108, wherein the pharmaceutical preparation is free of calcium or salts thereof.

117. (New) The pharmaceutical preparation of claim 116, wherein calcium, including ions thereof, is present in a concentration of less than 0.5%.

118. (New) The pharmaceutical preparation of claim 117, wherein calcium, including ions thereof, is present in a concentration of less than 0.1%.

119. (New) The pharmaceutical preparation of claim 118, wherein calcium, including ions thereof, is present in a concentration of less than 0.01%.

120. (New) The pharmaceutical preparation of claim 119, wherein there is no detectable level of calcium present.

121. (New) The pharmaceutical preparation of any of claims 116 - 120, wherein the preparation is an aqueous formulation comprising a chelating agent.